

Docket No.: C2432.0069

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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In re Patent Application of:

Ludger Grote et al.

Application No.: 10/598,114

Confirmation No.: 1212

Filed: July 3, 2007

Art Unit: 1617

For: METHOD OF TREATING AND  
DIAGNOSING SLEEP DISORDERED  
BREATHING AND MEANS FOR  
CARRYING OUT THE METHOD

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Examiner: Sahar Javanmard

**DECLARATION OF LUDGER GROTE, JAN HEDNER AND KAJ STENLOF**

**Ludger Grote, Jan Hedner and Kaj Stenlof** declare that:

1. We are the applicants in the above identified application.
2. We are aware that the United States Patent and Trademark Office has taken the position that because topiramate and zonisamide are both anti-convulsant agents and act as anti-convulsant agents by blocking sodium as well as T-type calcium channels, one would reasonably expect that the drugs could be substituted for one another and used to treat other conditions including OSA. This asserted "expectation" is not reasonable. It is necessarily based on the unspoken assumption that there is some relationship between OSA (on one hand) and blocking sodium and T-type calcium channels (on the other hand), but we are not aware of anything suggesting such relationship exists or even speculating that it might exist.

3. The "expectation" advanced by the Patent Office is based on a hypotheses that any patient treated with topiramate could also be treated with zonisamide. In order to evaluate this hypotheses, we clinically evaluated the effects in four patients consecutively exposed to both topiramate (50 mg b.i.d) and zonisamide (100 mg b.i.d). These dosage amounts were selected because they are considered equivalent when the drugs are used as an anticonvulsant. The sleep study was performed at steady state with treatment at 4 to 6 weeks after initiation of either therapy and the results are shown in the following Table where the designation (+) indicates a case in which there was a reduction of the apnea-hypopnea index by more than 50% and (-) indicates a reduction of less than 50%.

Patient number	1	2	3	4
Zonisamide	+	+	+	-
Topiramate	-	-	+	+

4. Our study found that three of the OSA patients responded to one of zonisamide and topiramate but not to the other. The fourth patient responded to both therapies. This data clearly shows that effects of these two compounds are unique and that a positive effect of one compound does not reasonably imply that the other agent will be effective. It shows that any commonality these drugs may have with respect to antiepileptic activity does not reasonably permit a prediction that zonisamide will be active in treating OSA because topiramate is active to treat this indication.

5. We hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated 11 July 2008

Dated 11 July 2008

Dated 11 July 2008

Ludger Grote

Ludger Grote

JAN HEDBERG

Jan Hedberg

Kaj Stenlof

Kaj Stenlof